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J. B. Segur

The Formation of oxazolons and  
Pentoxazolons and their Hydrolysis  
to Amino Alcohols



THE FORMATION OF OXAZOLONS AND PENTOXAZOLONS  
AND THEIR HYDROLYSIS TO AMINO ALCOHOLS

BY

JOHN BARTLETT SEGUR  
B. S. University of Illinois, 1919

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THESIS

Submitted in Partial Fulfillment of the Requirements for the

Degree of

MASTER OF SCIENCE

IN CHEMISTRY

IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1920



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JULY 31, 1920

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY  
SUPERVISION BY JOHN BARTLETT SEGUR

ENTITLED THE FORMATION OF OXAZOLONS AND PENTOXAZOLONS  
AND THEIR HYDROLYSIS TO AMINO ALCOHOLS.


BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR  
THE DEGREE OF MASTER OF SCIENCE.

Roger Adams In Charge of Thesis  
Roger Adams Head of Department

Recommendation concurred in\*

_____	}	Committee on Final Examination*
_____		
_____		

\*Required for doctor's degree but not for master's



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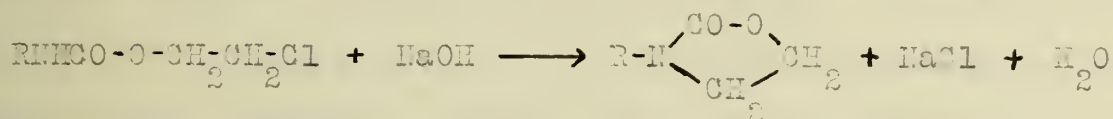
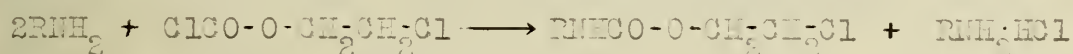


THE FORMATION OF OXAZOLONS AND PENTOXAZOLONS,  
AND THEIR HYDROLYSIS TO AMINO ALCOHOLS.

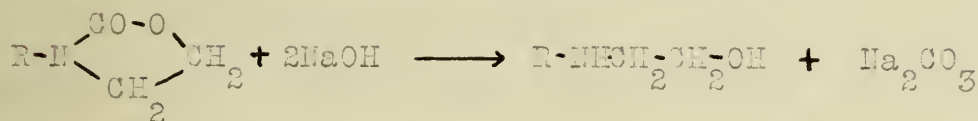
INTRODUCTION

The formation of oxazolons and pentoxazolons, and their hydrolysis to amino alcohols was studied in order to determine the best conditions for the reactions.

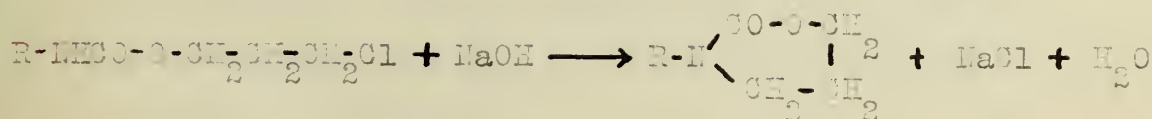
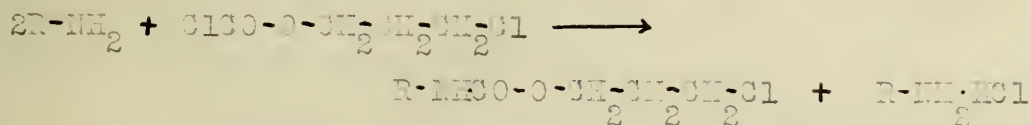
Oxazolons may be formed by condensing  $\beta$ -chloroethyl chlor-  
carbonate with a primary amine and refluxing the derivative of  
carbaminic acid that is formed with aqueous NaOH.



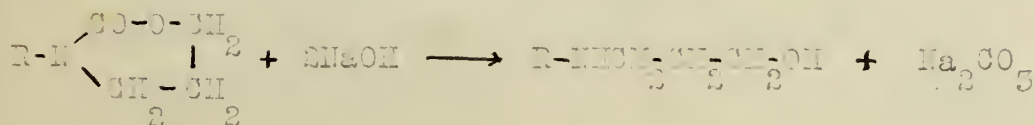
If an excess of NaOH is used and the refluxing is long continued,  
the oxazolon is hydrolyzed to an amino alcohol.



Pentoxazolons are formed in the same way by condensing  
 $\gamma$ -chloropropyl chlorocarbonate with a primary amine and refluxing  
the product with NaOH.



An excess of alkali hydrolyzes the pentoxazolon to an amino  
alcohol, if the refluxing is long continued.





### EXPERIMENTAL PART

Nemirowsky<sup>1</sup> made  $\beta$ -chloroethyl chlorocarbonate from phosgene and ethylene chlorohydrin. He condensed it with ammonia and with aniline and got the  $\beta$ -chloroethyl esters of the carbaminic acids. The N-phenyl carbaminic chloroethyl ester gave N-phenyl oxazolon when refluxed with concentrated KOH.

Paul Otto<sup>2</sup> continued the work of Nemirowsky. By refluxing phenyl carbaminic chloroethyl ester with saturated KOH he made hydroxyethyl aniline. He also made hydroxyethyl aniline by refluxing ethylene chlorohydrin with aniline. By using methoxy aniline and  $\alpha$  and  $\beta$  naphthalene in the place of aniline, the corresponding carbaminic esters, oxazolons and amino alcohols were formed. Hydroxyethyl aniline when treated with liquid phosgene in a sealed tube gave N-phenyl oxazolon.

The author<sup>3</sup> used the methods of Nemirowsky and prepared N-phenyl oxazolons and N-phenyl pentoxazolons with substituent groups on the phenyl ring. The pentoxazolons were made by condensing  $\gamma$ -chloropropyl chlorocarbonate with an aromatic amine and refluxing the carbaminic ester with NaOH. The  $\gamma$ -chloropropyl chlorocarbonate was prepared from phosgene and trimethylene chlorohydrin. The following compounds were made.

$\gamma$ -chloropropyl ester of phenyl carbaminic acid.

$\beta$ -chloroethyl ester of phenyl carbaminic acid.

N-phenyl oxazolon.

N-phenyl pentoxazolon.

$\beta$ -chloroethyl ester of o-tolyl carbaminic acid.

$\beta$ -chloroethyl ester of p-tolyl carbaminic acid.

N-p-tolyl oxazolon.





$\beta$ chloroethyl ester of p-ethoxy phenyl carbamic acid.

$\gamma$ chloropropyl ester of p-ethoxy phenyl carbamic acid.

11 p-ethoxy phenyl oxazolon.

11 p-ethoxy phenylpentoxazolon.

#### BIBLIOGRAPHY

- (1) Journ. E. Pract. Chemie (2) 51; 173-175.
- (2) " " " " (2) 44; 15-23.
- (3) The Formation of Oxazolon and Pentoxazolon Rings.  
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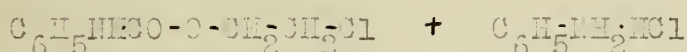
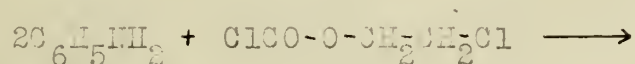




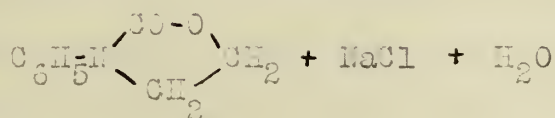
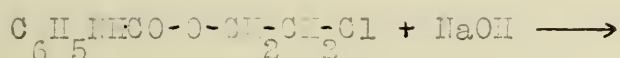
# THEORETICAL PART

Previous work has shown that it is possible to prepare substituted oxazolons and pentoxazolons; the substituent group being a phenyl or substituted phenyl group. N phenyl oxazolone has been hydrolyzed to hydroxyethyl aniline.

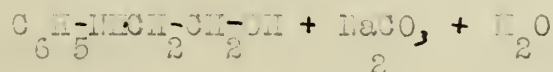
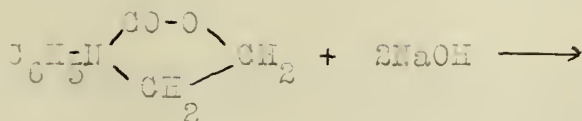
A series of experiments was made to find the best conditions for the reactions mentioned above, and to determine the effect of various substituent groups. The oxazolons were formed by condensing  $\beta$ -chloroethyl chlorocarbonate with a primary amine; for example, aniline.



The chloroethyl ester of phenyl carboninic acid loses HCl when refluxed with NaOH and forms N phenyl oxazolone.



An excess of NaOH hydrolyzes the N phenyl oxazolone to hydroxyethyl aniline.



Ortho and para-toluidine, o- and p-chloroaniline, and

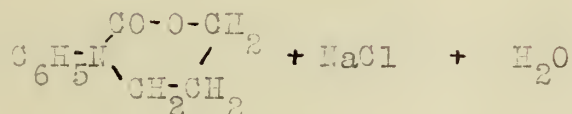
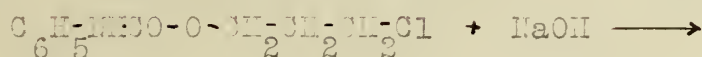
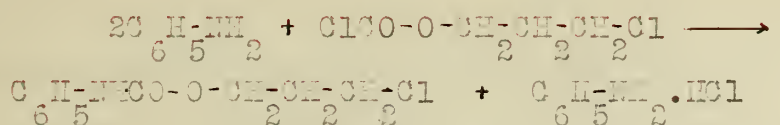


p-phenetidine were compared with aniline and it was found that the substituent groups had no effect other than slowing the speed of the reaction slightly. In all cases the amines condensed with the  $\beta$ -chloroethyl chlorocarbonate with the greatest ease. The oxazolons were best made by using an amount of NaOH just equivalent to the amount of ester used because an excess of NaOH hydrolyzes the oxazolon. Hydrolysis also took place to a slight extent if the NaOH solution was too concentrated. In the case of chloroethyl ester of phenyl carbaminic acid, the concentration should not be over 5%, but in all the other cases, a 25% solution will not be the cause of more than a slight hydrolysis of the oxazolon. The reaction mixtures were all refluxed for two hours. To obtain complete hydrolysis of the oxazolon, an excess of NaOH was necessary. Five moles of NaOH in a 33% solution, and one mole of the ester were found to give good results. The chloroethyl ester of phenyl carbaminic acid was completely converted to hydroxyethyl aniline after refluxing for two hours. The chloroethyl esters of o-tolyl, p-tolyl, and p-chlorophenyl carbaminic acids were completely changed to the corresponding hydroxyethyl amines after refluxing for four hours; but the esters of o-chloro- and p-ethoxy phenyl carbaminic acids gave a mixture of the oxazolon and hydroxyethyl amine after being refluxed for four hours.

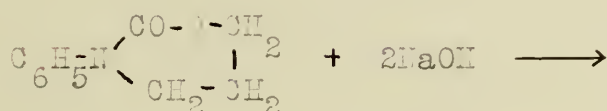
N substituted pentoxazolons were similar to N substituted oxazolons, both in their method of their formation and in the chemical properties. They may be formed by condensing  $\gamma$ -chloropropyl chlorocarbonate with a primary amine and then refluxing the chloropropyl ester of substituted carbaminic acid with NaOH.





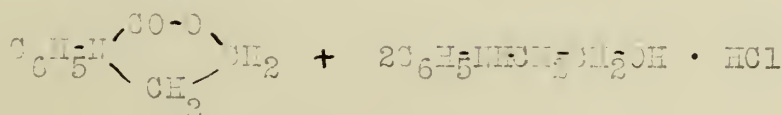
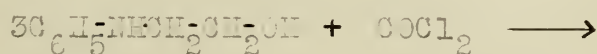


An excess of NaOH hydrolyzes the pentoxazolon to hydroxypropyl aniline.



Para-toluidine and aniline were used to make the pentoxazolon and it was found that varying the amount and concentration of the NaOH had the same effect upon the formation of the pentoxazolon ring and it's hydrolysis as with the oxazolons. Equivalent amounts of ester and NaOH in a 25% solution gave the pentoxazolon when refluxed two hours. One mole of ester and five moles of NaOH in a 33% solution gave a hydroxypropyl aniline when refluxed for four hours.

When hydroxyethyl aniline and phosgene are dissolved in an inert solvent such as benzene, they will react and form N phenyl oxazolon.







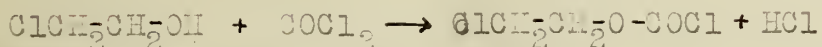
An attempt was made to prepare ethylene diphenyl urea with N phenyl oxazolon and aniline, but no reaction took place when the substances were refluxed together for eight hours.



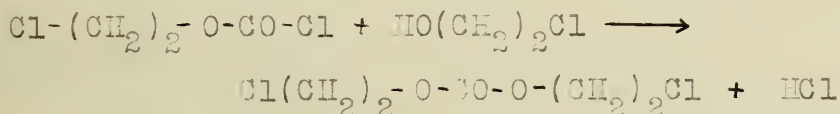
# EXPERIMENTAL PART

## I. Preparation of $\beta$ chloroethyl chlorocarbonate and $\delta$ chloropropyl chlorocarbonate.

$\beta$ chloroethyl chlorocarbonate was made by passing  $\text{COCl}_2$  into  $\text{ClCH}_2\text{CH}_2\text{OH}$  until the weight became constant.

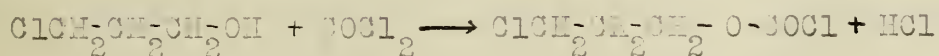


Because of the loss of the  $\text{HCl}$  the amount of  $\text{COCl}_2$  absorbed could not be accurately determined. It is necessary to cool the reaction flasks with ice and salt and to pass the  $\text{COCl}_2$  in slowly to prevent local heating. If the temperature rises or insufficient  $\text{COCl}_2$  is used,  $\text{Cl}(\text{CH}_2)_2\text{O-CO-O}(\text{CH}_2)_2\text{Cl}$  will be formed.



The product is washed with water, with dilute  $\text{Na}_2\text{CO}_3$  solution, and finally with water. It is then distilled. B. P.  $153^\circ$ . Specific gravity  $1.3856$   $25^\circ/20^\circ$ . It is a colorless liquid. The yields are from 80 to 85%. The  $\text{Cl}(\text{CH}_2)_2\text{O-CO-O}(\text{CH}_2)_2\text{Cl}$  boils at  $232^\circ - 235^\circ$ .

$\delta$ chloropropyl chlorocarbonate was made from  $\text{COCl}_2$  and  $\text{Cl}(\text{CH}_2)_3\text{OH}$  in the same way that  $\beta$ chloroethyl chlorocarbonate was made.



The same precautions against heating of the reaction mixture must be taken. The yields are from 80 to 85%. It is a colorless liquid; b. p.  $177^\circ$ ; sp. gr.  $1.2946$   $25^\circ/20^\circ$ ;  $n_D^{20} = 1.4456$ . Analysis; wgt. of sample .2512 g. wgt. of  $\text{AgCl}$  .4005g.



% of Cl; theory 45.10% ; observed, 44.90%.

## II. Preparation of the $\beta$ chloroethyl and $\gamma$ chloropropyl esters of substituted carbaminic acid.

The  $\beta$ chloroethyl esters and  $\gamma$ chloropropyl esters of the various carbaminic acids were all prepared in the same way.

### Preparation of chloroethyl ester of phenyl carbaminic acid.-

For each mole of  $\beta$ chloroethyl chlorocarbonate used, two moles of aniline were used. Each substance was dissolved in benzene and the two solutions were mixed slowly. The aniline hydrochloride precipitates from the benzene. Sufficient benzene was used so that the precipitate of aniline hydrochloride did not form a paste too thick to be stirred. The hydrochloride was filtered off, and the filtrate which contained the product was washed with dilute HCl and with water to remove all aniline and aniline hydrochloride. The benzene was then distilled off and the product crystallized when it cooled.

$C_6H_5NH_2$	1294 g.
$ClCH_2CH_2O-COCl$	944 g.
$C_6H_5NHCO-O-CH_2CH_2Cl$	1030 g.
% yield	78 %

It crystallized in white needles which were insoluble in water and soluble in alcohol and ether. M. P. 51°. Analysis; wgt. of sample .5320 g. The volume of  $H_2$  at 30° and 739.5mm. over 40% KOH was 22.0 cc. % of H; theory 7.01%; observed 7.40%.

### $\beta$ chloroethyl ester of o-tolyl carbaminic acid.

$o-CH_3-C_6H_4NH_2$	164 g.	50 g.	75 g.
$ClCH_2CH_2O-COCl$	110 g.	30 g.	50 g.
$o-CH_3-C_6H_4NHCO-O-(CH_2)_2Cl$	154 g.	18 g.	34 g.
% yield	76 %	60 %	46 %





The small yields of the smaller runs were due to the losses in crystallization. The product crystallized in white needles. It was very soluble in alcohol and ether, and slightly soluble in hot water. M. P. 45°. B. P. 209° - 210° at 37mm.

Analysis; wgt. of sample .4994 g. 50.3 cc. of  $H_2$  obtained at 29°, 743.4 mm. over 40% KOH. Percent of H; theory 6.55%, observed  $\frac{6.64}{6.55}$  %

$\beta$ chloroethyl ester of p-tolyl carbaminic acid.

$p-CH_3-C_6H_4-NH_2$	505 g.
$Cl(CH_2)_2-O-COCl$	355 g.
$p-CH_3-C_6H_4-NHCO-O-CH_2-CH_2-Cl$	403 g.
$\beta$ yield	80 %

The product crystallized in white flakes. It was very soluble in alcohol and ether, soluble in ligroin and slightly soluble in hot water. M. P. 61°. Analysis; wgt. of sample .3108 g. Wgt. of  $HgCl$  .2051 g.  $\beta$  Cl ; theory 16.60%, found 16.31%.

$\beta$ chloroethyl ester of o-chlorophenyl carbaminic acid.

$o-Cl-C_6H_4-NH_2$	132 g.	132 g.
$ClCH_2CH_2-O-COCl$	67 g.	67 g.
$o-Cl-C_6H_4-NHCO-O-CH_2-CH_2-Cl$	105 g.	73 g.
$\beta$ yield	83 %	57.5 %

The yield in the second run was low because the  $\beta$ chloroethyl chlorocarbonate used was impure. The product crystallized in white needles. It was very soluble in alcohol and ether and slightly soluble in hot water. M. P. 56.5° - 57°. Analysis; wgt. of sample .6106 g., 10.99 cc. of .8418 N acid used. % of H; theory 5.98%, observed 5.38%.





*p*-chloroethyl ester of *p*-ethoxyphenyl carbamic acid

$p\text{-C}_6\text{H}_4\text{-O-C}_6\text{H}_4\text{-NH}_2$	182 g.	46 g.
$\text{ClCH}_2\text{-CH}_2\text{-O-COCl}$	103 g.	17 g.
$p\text{-C}_6\text{H}_4\text{-O-C}_6\text{H}_4\text{-NHCO-O-(CH}_2\text{)}_2\text{-Cl}$	160 g.	40 g.
% yield	94 %	98 %

The product formed fine white crystals. It was very soluble in chloroform, benzene and ligroin, and slightly soluble in hot water.

M. P.  $94^\circ$ . Analysis; wgt. of sample .2689 g., wgt. of AgCl .1594 g. % of Cl; theory 14.55 %, observed 14.66 %.

*p*-chloroethyl ester of *p*-chlorophenyl carbamic acid.

$p\text{-ClC}_6\text{H}_4\text{-NH}_2$	50 g.	39 g.	100 g.
$\text{ClCH}_2\text{-CH}_2\text{-O-COCl}$	28 g.	50 g.	57 g.
$p\text{-ClC}_6\text{H}_4\text{-NHCO-O-(CH}_2\text{)}_2\text{-Cl}$	34 g.	75 g.	85 g.
% yield	74 %	92 %	92 %

The product crystallized in white needles. It was very soluble in alcohol and ether and slightly soluble in hot water.

M. P.  $65^\circ - 65^\circ$ . Analysis; wgt. of sample .3373 g., wgt. of AgCl .2900 g., % of Cl; theory 50.52 %, found 50.30 %.

*p*-chloroethyl ester of  $\alpha$ -naphthyl carbamic acid.

$\alpha\text{-C}_{10}\text{H}_7\text{-NH}_2$	35 g.
$\text{ClCH}_2\text{-CH}_2\text{-O-COCl}$	12.5 g.
$\alpha\text{-C}_{10}\text{H}_7\text{-NHCO-O-(CH}_2\text{)}_2\text{-Cl}$	11 g.
% yield	52 %

The product crystallized in white needles which melted at  $101^\circ - 101.5^\circ$ .



$\beta$ -chloroethyl ester of  $\beta$ -naphthyl carbamic acid.

$\beta$ -C <sub>10</sub> H <sub>7</sub> NH <sub>2</sub>	100 g.
ClCH <sub>2</sub> -CH <sub>2</sub> -O-COCl	50 g.
$\beta$ -C <sub>10</sub> H <sub>7</sub> NHCO-O-CH <sub>2</sub> -CH <sub>2</sub> -Cl	49 g.
% yield	38 %

The product crystallized in flat white crystals. M.P. 97.5° - 98°.

$\delta$ -chloropropyl ester of phenyl carbamic acid.

C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub>	150 g.	150 g.	150 g.
ClCH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-COCl	100 g.	100 g.	100 g.
C <sub>6</sub> H <sub>5</sub> NHCO-O-(CH <sub>2</sub> ) <sub>3</sub> -Cl	—	114 g.	120 g.
% yield	—	82 %	60 %

An attempt was made to distill the product of the first run, but it decomposed above 130° at 24 mm. In the next run the product was cooled with ice and salt. It crystallized in white needles. It was very soluble in alcohol and ether. The melting point was 54.5° - 55°.

$\delta$ -chloropropyl ester of p-tolyl carbamic acid.

p-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	210 g.	210 g.
ClCH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-COCl	150 g.	150 g.
p-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> NHCO-O-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -Cl	138 g.	40 g.
% yield	64 %	20 %

The product obtained after distilling off the benzene was a dark colored liquid which did not crystallize when cooled with ice and salt, and which could not be distilled without decomposition. Benzene was used as the solvent in the first run and ether was used in the second. The low yield in the second run was unaccounted for. A pure sample of the substance was not obtained.





### III. Preparation of Oxazolons, Pentoxazolons, and Amino Alcohols from Carbaminic Esters.

By varying the amount and concentration of the alkali that the carbaminic esters were refluxed with, the best conditions for the formation of the oxazolons or pentoxazolons and amino alcohols were found. The strength of the alkali solutions is expressed as percent KOH or NaOH by weight. At first, KOH was used, but NaOH was found to give the same results, so it was used. The NaOH was 95% pure.

Results of experiments on the preparation of 1-phenyl oxazolone and hydroxy thyl aniline.

Ratio of $C_6H_5NHCO-O-CH_2-CH_2-Cl$ to KOH		Gonc. of KOH	$C_6H_5NHCO-O-CH_2-CH_2-CH_2$ Crude grams		$C_6H_5NHCH_2-CH_2-CH_2$ Pure grams	
1:1	25g: 7g	1	13.0	60	0.0	—
1:1	25g: 7g	5	12.5	57.6	5.0	15.0
1:1	75g: 21g	20	36.0	55.0	19.5	25.0
1:1.5	25g: 10.5g	1	15.0	59.3	0.0	—
1:1.5	25g: 10.5g	2.5	15.0	68.7	0.0	—
1:1.5	25g: 10.5g	5	12.0	55.0	4.0	8.0
1:1.5	25g: 10.5g	10	13.5	62.0	4.0	12.0
1:1.5	25g: 10.5g	15	13.5	57.4	4.0	12.0
1:1.5	25g: 10.5g	20	13.5	57.4	4.0	12.0
1:1.5	25g: 10.5g	25	15.0	68.8	4.0	12.0
1:2	75g: 42g	30	51.5	48.2	25.5	55.0
1:5	25g: 21g	10	1.5	6.8	7.0	2.5
1:3	75g: 63g	25	5.0	7.6	31.5	61.5
1:4	75g: 84g	25	1.2	1.8	23.5	65.5
1:5	75g: 105g	20	0.0	0.0	39.5	75.0





In each case, the reaction mixture was refluxed two hours. The product was washed with water while still liquid, and the *p*-phenyl oxazolon crystallized on cooling. The hydroxyethyl aniline was filtered off. The oxazolon was dried and weighed. It may be recrystallized from hot water or hot alcohol. It formed white plates that were slightly soluble in hot water, and ether, and soluble in alcohol. M. P. 122°. The hydroxyethyl aniline was distilled at diminished pressure. It was a light yellow oil which darkens after standing. B. P. 167°- 170° at 19 mm., and 280°- 285° at atmospheric pressure. Sp. Gr. 1.1139 25/20°.  $n_D^{20} = 1.5749$ .

These experiments show that the *p*-phenyl oxazolon was formed without hydrolysis to hydroxyethyl aniline when one mole of KOH in a 1% solution was used with each mole of carbaminic ester. These same conditions were used in the preparation of the substituted *p*-phenyl oxazolons, pentoxazolons and amino alcohols.

Results of experiments on the preparation of *p*-tolyl oxazolon and hydroxyethyl *p*-toluidine.

Ratio of $\text{C}_6\text{H}_4(\text{CH}_2\text{NHCOC}_6\text{H}_4\text{NH}_2)\text{Cl}$ to NaOH	Conc. of NaOH	Time of reflux ing.	$\text{CH}_3\text{C}_6\text{H}_4\text{NHCOC}_6\text{H}_4\text{NH}_2$ Crude grams		$\text{CH}_3\text{C}_6\text{H}_4\text{NHCOC}_6\text{H}_4\text{NH}_2$ Pure grams		$\text{CH}_3\text{C}_6\text{H}_4\text{NHCOC}_6\text{H}_4\text{NH}_2$ %	
1:1 20g: 4g	1	2 hrs.	14.0	92.0	52.2	34.0	trace	
1:1 20g: 4g	2.5	2	11.7	75.0	4.4	29.0	trace	
1:1 20g: 4g	5	2	8.8	58.0	4.5	29.6	5.7	26.0
1:1 20g: 4g	10	2	10.0	66.0	7.0	46.1	2.6	16.0
1:1 50g:10g	25	2	42.0	100.0	39.0	94.0	trace	
1:3 50g:30g	50	2	37.5	98.0	25.0	60.5	trace	
1:4 50g:40g	25	2	42.0	100.0	36.0	68.0	trace	
1:5 50g:50g	33	4	0.0	0.0	0.0	0.0	26.0	73.5



The product of the reaction was washed with water while warm, and when it cooled, the hydroxyethyl p-toluidine was filtered off. The p-tolyl oxazolone was recrystallized from alcohol. It was slightly soluble in ether, ligroin and hot water, and crystallized from alcohol in white plates. M. P. 91°. The hydroxyethyl p-toluidine was distilled at diminished pressure. B. P. 153°-155° at 4mm. The distillate was a light yellow oil which crystallized in white needles which were very soluble in alcohol and ether, and slightly soluble in ligroin. It was recrystallized from a mixture of ether and ligroin. M. P. 43°-45°. Analysis; wgt. of sample .4475 g. 40.6 cc. of  $H_2$  obtained at 19°, 747.3mm., over 40% KOH. % of H; theory 9.27%, observed 9.28%.

Results of experiments on the preparation of N p-chlorophenyl oxazolone and hydroxyethyl p-chloroaniline.

Ratio of $C_6H_4-NO_2-CH_2-CH_2-Cl$ to $NaOH$	Conc. of $NaOH$	Time of reflux- ing	$C_6H_4-NO_2-CH_2-CH_2-Cl$ crude grams	pure grams	$C_6H_4-NO_2-CH_2-CH_2-Cl$ pure grams	
1:1 10g:3g	1%	2 hr.	6.7	74.0	5.2	35
1:1 25g:4.5g	25	2	—	—	20.5	90
1:3 30g:18g	30	2	22.0	89.0	16.0	59
1:5 30g:27g	33	4	00.0	0.0	0.0	0
1:5 30g:27g	40	4	—	—	14.0	52

The reaction products were washed with water and then heated with dilute HCl which dissolved the amino alcohol. The residue of N para-chlorophenyl oxazolone was recrystallized from hot alcohol. It formed white needle-like crystals which were soluble in alcohol and ether and slightly soluble in hot water. M. P. 118.5° - 119°. Analysis; wgt. of sample .4513 g. 8.74 cc. of





.2418 N acid used. % of N; theory 6.62%, observed 6.56%. The hydroxyethyl p-chloro-aniline hydrochloride was neutralized with NaOH and the free amino alcohol recrystallized from ether and ligroin. It crystallized in white needles. It was slightly soluble in ligroin and soluble in ether and alcohol. M. P. 77-77.5. Analysis; wgt. of sample .2241 g. 17.2 cc. of N obtained at 29° 743.4mm. over 40% KOH. % of N; theory 8.16%, observed 8.50%.

Results of experiments on the preparation of N p-ethoxyphenyl oxazolon and hydroxyethyl p-ethoxy aniline.

Ratio of $\text{C}_6\text{H}_4\text{-NHCOOCH}_2\text{CH}_2\text{Cl}$ $\text{C}_6\text{H}_5$ to NaOH	Conc. of NaOH	Time of reflux ing	$\text{C}_6\text{H}_4\text{-NHCOOCH}_2\text{CH}_2\text{Cl}$ $\text{C}_6\text{H}_5$ crude grams	$\text{C}_6\text{H}_4\text{-NHCOOCH}_2\text{CH}_2\text{Cl}$ $\text{C}_6\text{H}_5$ pure grams	$\text{C}_6\text{H}_4\text{-NHCH}_2\text{CH}_2\text{OH}$ $\text{C}_6\text{H}_5$ Pure grams
1:1 10g: 1.7g	15	2 hr.	8.0 94.0	3.2 36.0	0.0 0.0
1:1 41g: 7.1g	25	2	35.0 100.0	52.0 93.0	0.0 0.0
1:5 20g:11.0g	25	2	18.0 100.0	15.5 90.0	0.0 0.0
1:4 20g:15.0g	40	2	- -	11.0 65.0	5.8 55.6
1:5 25g:21g	33	2	- -	16.5 77.5	0.0 0.0
1:5 25g:21g	33	4	5.5 26.0	4.0 19.0	9.0 48.4

The reaction products were washed with water and then treated with dilute HCl which dissolved the amino alcohol. The residue of N p-ethoxy phenyl oxazolon was recrystallized from a mixture of alcohol and ether. It formed flaky white crystals which were very soluble in alcohol and benzene, soluble in ether, slightly soluble in hot water and very slightly soluble in ligroin.

M. P. 96°. The hydroxyethyl aniline hydrochloride was neutralized with NaOH and the amino alcohol recrystallized from dilute alcohol after being decolorized with bone-black. It formed very fine





flaky white crystals which are soluble in alcohol and ether.

M. P. 68.5° - 69°. Analysis; wgt of sample .3922 g. 23.0 cc. of H<sub>2</sub> obtained at 30°, 745.0mm. over 40% KOH. % of H; theory 7.73% observed 7.86%.

Results of experiments on the preparation of N o-tolyl oxazolon and hydroxyethyl o-toluidine.

Ratio of $\text{C}_6\text{H}_4\text{NHCOOCH}_2\text{CH}_2\text{Cl}$ CH <sub>3</sub> to NaOH	Conc. of NaOH	Time of reflux ing	$\text{C}_6\text{H}_4\text{NHCOOCH}_2\text{CH}_2\text{CH}_3$ CH <sub>3</sub> GRAMS %	$\text{C}_6\text{H}_4\text{NHCH}_2\text{CH}_2\text{OH}$ CH <sub>3</sub> GRAMS %
1:1 20g: 4g	1%	2 hr	9.8 54.0	0.5 0.0
1:1 50g:10g	25	2	15.0 42.5	0.5 1.4
1:3 50g:30g	25	2	57.0 65.0	3.5 10.0
1:5 25g:25g	35	4	3.0 14.5	9.5 52.5
1:5 30g:30g	40	2	16.0 64.5	1.5 4.2

The reaction products were washed with water and then heated with dilute HCl which dissolved the hydroxyethyl o-toluidine. The N o-tolyl oxazolon was a liquid, which was almost colorless when distilled at diminished pressure. It was soluble in alcohol and ether. Sp. Gr. 1.2024 25°/20°.  $n_D^{20}$  1.5503. B. P. 180°-185° at 3mm. Analysis; wgt. of sample .4145g. 31.8 cc. of H<sub>2</sub> obtained at 33°, 739mm. over 40% KOH. % of H; theory 7.92%, observed 8.09%. The hydroxyethyl o-toluidine hydrochloride was neutralized with NaOH and the free amino alcohol distilled at diminished pressure. It was a light yellow liquid, soluble in alcohol and ether. Sp. Gr. 1.0962 25°/20°.  $n_D^{20}$  1.5675. B. P. 145°-150° at 3mm. Analysis; wgt. of sample .5339 g. 29.3 cc. of H<sub>2</sub> obtained at 33°, 739mm., over 40% KOH. % of H; theory 9.27%, observed 9.25%.



Results of experiments on the preparation of *N* o-chlorophenyl oxazolon and hydroxyethyl o-chlorotoluene.

Ratio of $\text{C}_6\text{H}_4\text{NHCOCCH}_2\text{CH}_2\text{Cl}$ to NaOH	Conc. of NaOH	Time of reflux ing	$\text{C}_6\text{H}_4\text{NHCOCCH}_2\text{CH}_2\text{Cl}$ pure grams	$\text{C}_6\text{H}_4\text{NHCOCCH}_2\text{CH}_2\text{OH}$ pure grams
1:1 15g: 3g	15	2 hr	4.5	55.0
1:1 30g: 6g	25	2	19.0	70.0
1:3 30g:18g	30	2	18.5	18.5
1:5 30g:27g	33	4	4.0	14.5
			11.0	50.0

The reaction products were washed with water and the hydroxyethyl o-chloroaniline was extracted with dilute HCl. The *N* o-chlorophenyl oxazolon was a liquid having a slight yellow tint. It was soluble in alcohol and ether. Sp. Gr. 1.2500 25°/20°.  $n_D^{20}=1.5640$ . B.P. 185°-188° at 3mm. Analysis; wgt. of sample .7051. 13.17 cc. of .2418 N acid used. % of N; theory 6.62%, observed 6.32%. The hydroxyethyl o-chloroaniline was a light yellow oil which was soluble in alcohol and ether. Sp. Gr. 1.2576 25°/20°.  $n_D^{20}=1.5185$ . B. P. 148°-152° at 3mm. Analysis; wgt. of sample .4348 g. 9.71 cc. of .2418 N acid used. % of N; theory 8.16%, observed 7.58%.

*N* αnaphthyl oxazolon and *N* βnaphthyl oxazolon were prepared, but as only one run of each was made their behavior cannot be compared with that of the other oxazolons. The same method of preparation used in the previous experiments were used here.

Seven grams of  $\text{C}_{10}\text{H}_7\text{NHCOCCH}_2\text{CH}_2\text{Cl}$  and 8.5 grams of KOH in a 33% solution were refluxed for 1 hour. The  $\text{C}_{10}\text{H}_7\text{NHCOCCH}_2\text{CH}_2\text{Cl}$  was recrystallized from hot alcohol. It formed flat white crystals which were soluble in alcohol and slightly soluble in ether.





M. P. 126°-127°. Yield 5 g.; 84%. No hydroxyethyl  $\alpha$  naphthyl amine was formed.

Seven grams of  $\beta$ -C<sub>10</sub>H<sub>7</sub>NHCOOCH<sub>2</sub>CH<sub>2</sub>Cl and 8.5 g. of KOH in a 55% solution were refluxed for 1 hour. After being washed with water, the product was dissolved in benzene. Two volumes of ligroin were added and the product crystallized on cooling. It formed flat crystals which were very slightly soluble in cold alcohol, ether, ligroin, and carbon tetrachloride. It was slightly soluble in hot alcohol and is soluble in hot benzene. M.P. 185°-186°. Yield 2g.; 34%. No hydroxyethyl  $\beta$  naphthyl amine was formed.

N substituted pentoxazolons are quite similar to the N substituted oxazolons. The same methods were used in studying them as were used with the N substituted oxazolons.

Results of experiments on the preparation of N phenyl pentoxazolons and hydroxypropyl aniline.

Ratio of C <sub>6</sub> H <sub>5</sub> NHCOOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> Cl to NaOH	Conc. of NaOH	Time of reflux ing	C <sub>6</sub> H <sub>5</sub> NHCOOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> Cl pure grams	C <sub>6</sub> H <sub>5</sub> NHCOOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> Cl pure grams
1:1 50g:10g	25%	2 hr	53.0	80.0
1:5 44g:43g	40	2	13.0	42.0
1:5 50g:50g	55	4	0.0	0.0

The reaction product was washed with water and the hydroxypropyl aniline extracted with dilute HCl. The N phenyl pentoxazon was recrystallized from hot alcohol. It crystallized in the form of white needles. It was soluble in hot water, alcohol, ether and benzene, and was very slightly soluble in ligroin. M. P. 95°. The hydroxypropyl aniline was distilled at reduced





pressure. It was a colorless liquid, soluble in alcohol and ether. Sp. Gr. 1.0873 25°/20°.  $n_D^{20} = 1.5679$ . B. P. 150°-155° at 5mm. Analysis; wgt. of sample .3592 g. 6.18 cc. of .2418 N acid used. % of H; theory 9.27%, observed 4.07%.

Results of experiments on the preparation of 1 p-tolyl pentoxazolon and hydroxypropyl p-toluidine.

Ratio of $\text{C}_6\text{H}_4\text{NHCOO}(\text{CH}_2)_3\text{Cl}$ to NaOH	Conc. of NaOH	Time of reflux ing	$\text{CH}_3\text{C}_6\text{H}_4\text{NHCOOCH}_2\text{CH}_2\text{CH}_2\text{OH}$ crude grams	$\text{CH}_3\text{C}_6\text{H}_4\text{NHCH}_2\text{CH}_2\text{CH}_2\text{OH}$ pure grams	$\text{C}_6\text{H}_4\text{NHCH}_2\text{CH}_2\text{CH}_2\text{OH}$ pure grams
1:1 20g: 3.7g	25%	2 hr	9.0	55.5	3.0 18.0
1:5 20g:18.0g	33	4	0.0	0.0	0.0 0.0
1:5 78g:70.0g	40	2	-	-	17.0 26.0
					31.0 70.0

The reaction products were washed with water and the 1 p-tolyl pentoxazolon was recrystallized from hot alcohol. It crystallized in white needles which were very soluble in alcohol, and slightly soluble in ether and hot water. M. P. 127°-128°. Analysis; wgt. of sample .7887 g. 54.7 cc. of  $\text{H}_2$  obtained at 27.5°, 747mm. over 40% KOH. % of H; theory 7.23%, observed 7.38%. The hydroxypropyl p-toluidine was distilled under diminished pressure. It was a light yellow liquid, soluble in alcohol and ether. Sp. Gr. 1.0672 25°/20°.  $n_D^{20} = 1.5567$ . B. P. 155°-165° at 5mm. Analysis; wgt. of sample .3001 g. 3.48 cc. of .2418 N acid used. % of H; theory 8.48%, observed 5.93%.

In the distillation of the amino alcohol from the second run there was about three grams of a thick red residue. This was about 30% of the total product. It was dissolved in HCl, and when neutralized with NaOH, the oil obtained was the original hydroxypropyl toluidine. Apparently polymerization had taken place



during the distillation.

#### IV. Preparation of Hydroxyethyl Aniline and Hydroxy-o-chloro Aniline.

Some hydroxyethyl aniline was made from ethylene chlorohydrin and aniline. Two hundred and fifty grams of aniline, 178 g. of ethylene chlorohydrin, and 200g. of sodium carbonate were refluxed together for 5 hours. The liquid was filtered from the  $\text{Na}_2\text{CO}_3$  and NaCl and distilled at atmospheric pressure.

Fraction I	179° - 185°	64 g.
II	<u>185° - 195°</u> - 205°	40 g.
III	205° - 275°	45.5 g.

These fractions were refractionated at reduced pressure.

Fraction I	77° - 78° at 12 mm.	55.5 g.
II	150° - 155° at 7.5 mm.	57.5 g.
III	Residue	6.0 g.

Yield; 57.5 g., 21.5%.

This method gave such poor results that it was not used.

Hydroxyethyl o-chloroaniline was made in the same way with similar results. One hundred and ninety-one grams of o-chloro-aniline, 80.5 g of ethylene chlorohydrin and 106 g. of sodium carbonate were refluxed for 5 hours. The liquid was filtered off and distilled at atmospheric pressure.

Fraction I	74° - 78°	at 8 mm.	120 g.
II	79° - 144°	at 7 mm.	9 g.
III	144° - 145°	at 6 mm.	25.5 g.

Yield 25.5 g., 14.9%.





V. Action of Aniline on N Phenyl Oxazolon.

N phenyl oxazolon was refluxed with aniline in an attempt to make ethylene diphenyl urea. Twenty five grams of N phenyl oxazolon and 28.6 g. of aniline (1 mole to 2 moles) were refluxed for eight hours but ~~no~~<sup>no</sup> reaction took place. The N phenyl oxazolon was recovered unchanged.

VI. Preparation of N Phenyl Oxazolon from Hydroxyethyl Aniline and Phosgene.

N phenyl oxazolon was made from hydroxyethyl aniline and phosgene. An excess of  $\text{COCl}_2$  was passed into 37.5 g. of hydroxyethyl aniline dissolved in 300 cc. of benzene. The solution became milky at first but soon cleared up. An orange yellow oil separated below the benzene. This was drawn off, and on cooling fine white crystals formed in it. The oil was diluted with alcohol and filtered from the crystals. The crystals were washed with alcohol and ether. Their melting point was  $120^{\circ}$ - $121^{\circ}$ . They were N phenyl oxazolon. The yield was only 1.6 g. The oil boiled at  $182.5^{\circ}$  at 17mm.

In the second run 59 g. of hydroxyethyl aniline were dissolved in 100 cc. of benzene and 14 g. of phosgene were dissolved in an equal amount of benzene. The two solutions were mixed slowly and a layer of liquid separated under the benzene. The benzene was distilled off, and after standing for two days, the residue was a paste of white crystals and oil. The oil was filtered off and the crystals which were N phenyl oxazolon, were recrystallized from water. M.P.  $112^{\circ}$ - $119^{\circ}$ . Mixed melting point with N phenyl oxazolon,  $118^{\circ}$ - $120^{\circ}$ . Yield 11 g., 48% of theory. The oil that was formed boiled with decomposition at 175 mm. pressure.

Note: The temperatures recorded in this thesis are uncorrected





for the stem exposure of the thermometer.



SUMMARY

$\beta$ -chloroethyl chlorocarbonate was condensed with primary aromatic amines to form  $\beta$ -chloroethyl esters of substituted carbanilic acid. By refluxing with NaOH, these esters lost HCl and substituted oxazolons were formed. The oxazolons were hydrolyzed by an excess of alkali to hydroxyethyl amines. Equimolecular amounts of the ester and of NaOH in a 15% solution give the best yields of the oxazolons. An excess of NaOH favors the hydrolysis of the oxazolons. The hydrolysis takes place more readily in a concentrated solution than in a dilute solution. By using one mole of ester and 5 moles of NaOH in a 33% solution, good yields of hydroxyethyl amines were obtained. The speed of the reactions varied. If phenyl oxazolone and hydroxyethyl aniline were formed most easily. A substituent group on the benzene ring made the reactions go slower. The compounds having methyl and Cl radicals in the ortho and para positions and the ethoxy group in the para position were made. Neither the nature of the group nor its position varied the effect upon the reaction.

$\delta$ -chloropropyl chlorocarbonate was condensed with primary aromatic amines to form  $\delta$ -chloropropyl esters of substituted carbanilic acid. By refluxing with NaOH these esters lost HCl, and formed substituted pentoxazolons. The pentoxazolons were hydrolyzed by an excess of alkali to basic compounds. The method of formation and such of their chemical and physical properties as were observed would indicate that these basic compounds were hydroxypropyl amines with the formulae given. However, analysis showed that their nitrogen content was approximately one half of that required by the formulae used. The true formulae of these



compounds were not determined.

Hydroxyethyl amines were made by the reaction of an aromatic amine and ethylene chlorohydrin, but the yield was poor.

N phenyl oxazolon and aniline did not react when refluxed together.

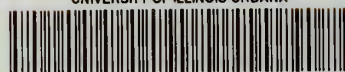
Hydroxyethyl aniline and phosgene reacted and formed N phenyl oxazolon. A liquid by-product was also formed.







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